REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and these comments.

Cancellation of claims 3, 17 and 28 is requested, without prejudice or disclaimer thereto. As to claims 2, 4-12, 15, 18, 19, 24, 25 and 27, revisions are presented that are essentially of a clarifying nature and otherwise amply supported by the original specification.

Upon entry of this response, claims 2, 4-12, 15, 16 and 18-27 will be pending.

I. Claim Objections

Claims 2-12, 19, 24 and 28 were objected to for reciting various phrases. Although applicants respectfully traverse this objection, the following changes have been made above, solely to expedite prosecution,.

a) Claim 2 was objected to as being unclear due to the wording "harmful substances responsible of inducing sepsis." The present invention relates to removal of harmful substances responsible of inducing sepsis caused by Gram-negative bacteria or Gram-positive bacteria by using an absorption method with particles having affinity for i) the LPS portion of Gram-negative bacteria and/or ii) Gram-positive bacteria or harmful substances derived from said Gram-positive bacteria. It would be clear to a person skilled in the art which substances are responsible of inducing sepsis caused by Gram-negative or Gram-positive bacteria and thereby which substances are covered by the term "harmful substances responsible of inducing sepsis." This also is made clear in the claim, since the absorption method is based on an adsorption medium characterized by having specific affinity towards the LPS portion of Gram-negative bacteria and/or ii) Gram-positive bacteria or harmful substances derived from said Gram-positive bacteria, and in the description (paragraph [0065]) where the term "harmful substance derived from Gram-positive bacteria" is defined as an entity promoting the development of sepsis and being either a constituent of Gram-positive bacteria or a secondary species to Gram-positive bacteria causing sepsis.

b) Dependent claims 3-12, 19 and 24 refer to "A method." This has been corrected to "The method," in compliance with the examiner's suggestion.

c) Claims 3 and 17 were objected to under 37 CFR 1.75(c), as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Without acquiescing to the objection, applicants have canceled these claims.

II. Claim Rejections under 35 U.S.C. § 112

Claims 2-12 and 27-28 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

a) The term "being effected" in claims 2 and 27 have been replaced with "comprising."

b) The phrase "such as" in claims 5, 12, 15, 18 and 25 have been deleted.

c) "Preferably," "most preferably" and "most preferred" have been deleted from claims 5, 11, 18 and 24.

d) Use of "i.e." is discontinued in claims 12 and 25, clarifying the qualifications of the claimed invention.

e) The phrase "in particular" in claim 4 have been deleted.

f) Claims 11 and 24 have been amended to recite the alternative recitations in Markush-group manner.

Furthermore, claims 2 and 27 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting essential steps; namely, a contact step between the affinity specific molecule and the bacteria and a correlation step which correlates treating blood by passing the blood through the column assembly and acquiring an extracorporeal adsorption method for removing harmful substances responsible of inducing sepsis caused by bacteria. These steps have been included by adding the text "removing the harmful substances from the blood by binding of the harmful substances to the affinity specific molecules and thereby retaining them in the column" to claims 2 and 27. Support for this amendment can be found throughout the specification, particularly in paragraph [0122]].

III. Claim Rejections under 35 U.S.C. § 102

Lihme

Claims 2-9, 11-12, 15-22 and 24-28 have been rejected for alleged anticipation by Lihme, WO 02/053251. Applicants respectfully traverse this rejection.

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or *described in a printed publication* in this or a foreign country, before the invention thereof by the applicant for a patent.

35 U.S.C. § 102 (emphasis added). For Section 102(a) to apply, the reference must have a publication date earlier in time than the effective filing date of the application, and must not be applicant's own work. MPEP § 706.02(a). A reference is proven to be a "printed publication" "upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it." MPEP § 2128 (citations omitted).

Pursuant to these criteria, a PCT application is only available to the public upon publication. See the table in MPEP § 901.05, explaining the date of public access for various types of foreign patents.

Because it has a publication date of July 11, 2002, Lihme is not Section 102(a) prior art against the present application. The present application has a priority date of July 11, 2002, which has been perfected under 35 U.S.C. § 119, as the summary attached to the instant Office Action acknowledges. Since the publication date of the cited application is not earlier than the date of the perfected priority claim of the present application, the cited application is not prior art under 35 U.S.C. § 102(a). Accordingly, applicants respectfully request that the rejection be withdrawn.

Zimmerman et al.

Claims 2-8, 11-12, 15-18, 20-21 and 24-28 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Zimmerman et al (US 6,090,292). Applicants respectfully traverse this rejection.

An rejection for anticipation under Section 102 requires a showing that each limitation of a claim is found in a single reference, practice or device. *See In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985). In order for a reference to be anticipatory, it must "be enabling and describe the applicant's claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention." *See In re Paulsen*, 30 F.3d 1475 (Fed. Cir. 1994). Applicants assert that the cited references do not anticipate the present claims as they do not teach each and every element of the claims.

Zimmerman *et al.* discloses a method based on plastic (particles, film or hollow fiber) coated with albumin. This method takes advantage of the fact that albumin can be used as a ligand for removing toxins from blood or plasma. Zimmerman *et al.* discloses the use of packed columns [col. 3 line 23; col. 4 lines 48] and not fluidized columns as in the present application [claim 2 and 27 of the pending claims]. There is no teaching on how to construct a perfusable packing from 10-500 μm beads. Instead, examples of batchwise adsorption of whole blood are disclosed [col. 3 line 64+], while examples with packed columns comprise plasma pumped at a flow rate of only 2 ml/min [col. 4 line 45+] and heparinised whole blood perfused at 0.5 ml/min only [col. 6, table].

Thus, the Zimmerman patent does not disclose the removal of bacteria or other bio-macromolecular entitles from blood only protein-bound toxins. This is in contrast to the present invention which in addition to binding and depleting the blood of soluble, harmful substances, the specific bio-macromolecular entitles being bound by the affinity-specific molecules of the fluidized bed will also be bound when present on cells in the blood stream (compare pending claim 2 and 27).

Since Zimmerman *et al.* does not teach each and every element of the claimed invention, it cannot anticipate the claims. Accordingly, the rejection should be withdrawn.

Jaber et al.

Claims 2-7, 10, 16-18, 20, 23 and 26-28 have been rejected for alleged anticipation over Jaber *et al.*, American Journal of Kidney Diseases. Vol. 30, No. 5, Suppl. 4, 1997: pages S44-S56. Applicants respectfully traverse this rejection.

Jaber *et al.* reviews extracorporeal adsorbent-based strategies in sepsis. Jaber describes the use of Polymyxin B-coated fibers, macroporous cellulosic beads and sepharose-

solid-phase columns [page S45 table 1, page S48+]. The use of a fluidized bed [claim 2 and 27 of the pending claims] is not described or taught by Jaber *et al.* The reference describes an antibody-coated microspheres detoxification system (MDS) which is very different from the current invention [page S53 col. 1]. The microspheres are microparticles with a diameter of 0.1-5 μm [page S52 col. 2]. Furthermore two extracorporeal circuits connected by a plasma filter is needed to circumvent direct contact between blood cells and microparticles, and a high-velocity centrifugal pump is necessary to keep the microparticles in suspension and circulation [page S53 col. 1].

This system of Jaber *et al.* differs significantly from the present invention. Jaber *et al.* does not teach or suggest a method for removing toxins from blood, based on the assembly of an adsorption column with such a flow rate that a fluidised bed of particles is formed, using molecules with a specific affinity for bacteria or bacteria-derived substances [see pending claim 2 and 27]. Furthermore, Jaber *et al.* does not suggest the use of a combination of molecules with a specific affinity along with the use of a fluidized bed.

It is apparent, therefore, that Jaber *et al.* does not teach each and every element of the claimed invention. It cannot anticipate the claims, therefore, the rejection should be withdrawn.

CONCLUSION

Applicants submit that the present application is in condition for allowance. Favorable reconsideration of the application as amended is requested, therefore. Examiner Hines is invited to contact the undersigned directly, should he feel that any issue warrants further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, then applicants hereby petition for such extension under 37 CFR § 1.136 and authorizes payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

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